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AHA Policy Statement

Regional Systems of Care for Out-of-Hospital Cardiac Arrest

A Policy Statement From the American Heart Association

Graham Nichol, MD, MPH, FAHA, Chair; Tom P. Aufderheide, MD, FAHA; Brian Eigel, PhD; Robert W. Neumar, MD, PhD; Keith G. Lurie, MD; Vincent J. Bufalino, MD, FAHA; Clifton W. Callaway, MD, PhD; Venugopal Menon, MD, FAHA; Robert R. Bass, MD; Benjamin S. Abella, MD, MPhil; Michael Sayre, MD; Cynthia M. Dougherty, PhD, FAHA; Edward M. Racht, MD; Monica E. Kleinman, MD; Robert E. O'Connor, MD; John P. Reilly, MD; Eric W. Ossmann, MD; Eric Peterson, MD, MPH, FAHA; on behalf of the American Heart Association Emergency Cardiovascular Care Committee; Council on Arteriosclerosis, Thrombosis, and Vascular Biology; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Cardiovascular Nursing; Council on Clinical Cardiology; Advocacy Committee; and Council on Quality of Care and Outcomes Research

Endorsed by the National Association of State EMS Officials

Abstract*—**Out-of-hospital cardiac arrest continues to be an important public health problem, with large and important regional variations in outcomes. Survival rates vary widely among patients treated with out-of-hospital cardiac arrest by emergency medical services and among patients transported to the hospital after return of spontaneous circulation. Most regions lack a well-coordinated approach to post–cardiac arrest care. Effective hospital-based interventions for out-of-hospital cardiac arrest exist but are used infrequently. Barriers to implementation of these interventions include lack of knowledge, experience, personnel, resources, and infrastructure. A well-defined relationship between an increased volume of patients or procedures and better outcomes among individual providers and hospitals has been observed for several other clinical disorders. Regional systems of care have improved provider experience and patient outcomes for those with ST-elevation myocardial infarction and life-threatening traumatic injury. This statement describes the rationale for regional systems of care for patients resuscitated from cardiac arrest and the preliminary recommended elements of such systems. Many more people could potentially survive out-of-hospital cardiac arrest if regional systems of cardiac resuscitation were established. A national process is necessary to develop and implement evidence-based guidelines for such systems that must include standards for the categorization, verification, and designation of components of such systems. The time to do so is now. (Circulation*. 2010;121:00-00.**)

Key Words: AHA Scientific Statements ■ emergency medicine ■ cardiac arrest

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The contributors to this statement were selected for their expertise in the disciplines relevant to cardiac resuscitation and post–cardiac arrest care. They represent several major professional groups whose practices are relevant to resuscitation care. These groups were contacted and agreed to provide contributors. Planning was initially conducted by e-mail, and invitations were issued. After a series of telephone conferences between the chair and members of the writing group, writing teams were formed to generate the content of each section. The chair of the writing group assigned individual contributors to work on 1 or more writing teams that generally reflected their area of expertise. Articles and abstracts presented at scientific meetings relevant to regional systems of cardiac resuscitation care were identified through PubMed, EMBASE, and an American Heart Association EndNote master resuscitation reference library and supplemented by manual searches of key papers. Drafts of each section were written and agreed on by members of the writing team and then sent to the chair for editing and incorporation into a single document. The first draft of the complete document was circulated among writing team leaders for initial comments and editing. A revised version of the document was circulated among all contributors, and consensus was achieved before submission of the final version for independent peer review and approval for publication.

Background

Out-of-hospital cardiac arrest (OOHCA) is a common, lethal public health problem that affects 236 000 to 325 000 people in the United States each year.[1] If deaths due to OOHCA were separated from deaths due to other cardiovascular causes, OOHCA would be the third-leading cause of death. There is at least a 5-fold regional variation in the outcome of OOHCA patients treated by emergency medical services (EMS) personnel among sites participating in the Resuscitation Outcomes Consortium.[1] Large interhospital variations exist in survival to hospital discharge after admission after successful resuscitation from OOHCA.[2–4] Such differences do not appear to be explained by differences in patient characteristics, which implies that variation in hospital-based care contributes to differences in outcomes across regions. Therefore, large opportunities remain to improve outcomes after cardiac arrest.

Certain care processes have been demonstrated to improve patient outcomes after successful resuscitation from OOHCA. Although therapeutic hypothermia was shown to improve outcomes in comatose survivors of out-of-hospital ventricular fibrillation (VF), it is used infrequently in the United States.[5] A perceived barrier to its use is lack of knowledge about and experience with therapeutic hypothermia.

Organized hospital-based care of patients resuscitated from OOHCA can achieve important improvements in outcome.[6] For example, percutaneous coronary intervention (PCI) is feasible and is associated with good short-term outcomes after cardiac arrest,[6–12] as it is for patients with acute myocardial infarction. Implantable cardioverter-defibrillators (ICDs) are known to be effective in patients who have experienced life-threatening arrhythmias but are implanted in only a minority of such patients.[13]

The American Heart Association Emergency Cardiovascular Care Programs and other organizations have invested considerable time, effort, and resources in developing and disseminating evidence-based resuscitation guidelines and training materials to improve the outcome of OOHCA. Despite these efforts, an increased rate of success of cardiac resuscitation over time has been difficult to detect.[14–16] This is due in part to the absence of a uniform approach to monitoring and reporting outcomes of OOHCA.[17] In contrast to the lack of improvement in survival after OOHCA, implementation of regional systems of care for those with traumatic injury[18] and acute myocardial infarction[19–21] has led to significant and important improvements in outcomes for patients with these conditions. Acute stroke care is also being reorganized into regional systems. The time has come to develop and implement regional systems of care for patients resuscitated from OOHCA to try to achieve similar improvements in outcomes. Regionalization of care should improve implementation of intra-arrest and postarrest interventions for patients who receive care in these systems.

This statement describes the rationale for regional systems of care for patients with OOHCA. Existing models of regional systems of care for OOHCA, traumatic injury, ST-elevation myocardial infarction (STEMI), and stroke are critiqued, and the essential components of regional systems of care for patients with OOHCA are discussed. These efforts are aimed at improving outcomes but may not always be feasible because of limited resources or other factors. Changes in care delivery, legislation, and reimbursement are likely necessary to maximize the impact of regional systems of cardiac resuscitation on public health.

Regional Systems of Care for Patients With OOHCA

Current State

As of April 2009, few American regions have implemented cardiac resuscitation systems of care to improve outcomes after OOHCA (eg, Arizona and parts of Minnesota, New York, Ohio, Texas, and Virginia). Those that exist have usually developed ad hoc, without comprehensive evidence-based criteria, common standards, or dedicated reimbursement. Some institutions have designated themselves as resuscitation centers of excellence that may or may not be part of a regional system. Some regions have attempted to create a system of care by transporting patients resuscitated in the field from OOHCA only to hospitals capable of inducing hypothermia,[22] but other regions have been unable to do so.[23] Furthermore, there is no published evidence of the impact of such programmatic interventions on the structure, process, or outcome of cardiac resuscitation, because regional systems of care for

Table 1. Effectiveness of Multifaceted Post–Cardiac Arrest Interventions

Authors/Reference: Design	Population	Intervention	Comparator
Oddo et al[35]: Case-control	Prop. VF: 79%	Hypothermia, PPCI, goal-directed therapy, glucose control not stated (n=55)	Standard care (n=54)
	Outcome for VF subgroup*	CPC 1 or 2 at discharge: 20 (37%)	CPC 1 or 2 at discharge: 6 (11%); P=0.004
Sunde et al[6]: Case-control	Prop. VF: 90%	Hypothermia, PPCI, goal-directed therapy, glucose control (n=61)	Standard care (n=58)
		CPC 1 or 2 at discharge: 56%	CPC 1 or 2 at discharge: 26%; P=0.001
Knafelj et al[7]: Case-control	STEMI Prop. VF: 100%	Hypothermia, PPCI, goal-directed therapy, glucose control not stated (n=40)	Standard care (n=32)
		CPC 1 or 2 at discharge: 53%	CPC 1 or 2 at discharge: 19%; P=0.001
Wolfrum et al[11]: Case-control	STEMI Prop. VF: 100%	Hypothermia, PPCI, goal-directed therapy, glucose control not stated (n=16)	Standard care (n=17)
		CPC 1 or 2 at discharge: 69%	CPC 1 or 2 at discharge: 47%. P=0.3
Gaieski et al[37]: Case-control	Prop. VF: 50%	Hypothermia, PPCI, goal-directed therapy, glucose control (n=20)	Standard care (n=18)
		CPC 1 or 2 at discharge: 8 (40%)	CPC 1 or 2 at discharge: 4 (22%)

Prop. VF indicates proportion with ventricular fibrillation; PPCI, primary percutaneous coronary intervention; and CPC, cerebral performance category.
*Hemodynamic goals achieved within 6 hours of presentation in emergency department.

OOHCA have not been evaluated formally. Therefore, we summarize evidence of the effectiveness of out-of-hospital and hospital-based interventions for OOHCA and extrapolate from evidence of the effectiveness of regional systems of care for other related disorders.

Evidence of Effectiveness of Multifaceted Out-of-Hospital Interventions

Since the advent of emergency cardiovascular care more than 40 years ago, treatment strategies to improve outcomes after OOHCA have focused primarily on early access to 9-1-1, the training of laypeople to perform cardiopulmonary resuscitation,[24] public access defibrillation,[25] dispatcher-assisted cardiopulmonary resuscitation,[26] first-responder defibrillation,[27] and improvements in the provision of advanced cardiovascular life support by paramedics.[28] Compared with a median reported survival-to-discharge rate of 8.4% for EMS-treated cardiac arrest by EMS systems throughout North America,[1] Seattle and King County, Wash, has achieved a 16.3% survival rate after any initial rhythm and a 39.9% survival-to-discharge rate after VF.[1] Similarly, Rochester, Minn, has achieved a 46% survival-to-discharge rate after bystander-witnessed VF.[29] Recently, several cities have implemented multiple simultaneous changes to EMS care for OOHCA. These changes are associated with increased rates of survival to discharge.[4,30–33] These observations suggest that hospitals will receive an increasing number of patients resuscitated from OOHCA who require timely, advanced, definitive care to ensure that they are discharged from the hospital alive and neurologically intact.

Evidence of Effectiveness of Multifaceted Post–Cardiac Arrest Interventions

Many patients who are initially resuscitated from OOHCA and admitted to the hospital die before discharge or have residual neurological impairment.[34] Although intra-arrest care has been the traditional focus of clinical investigation and resuscitation treatment guidelines, more recent efforts have revealed the importance of post–cardiac arrest care.[34] Management is further complicated by the logistics of patient care. Patients resuscitated from OOHCA are transported to multiple physical locations for treatment by diverse healthcare providers but require time-sensitive interventions that are continuously available. Hospital-based providers often treat postarrest patients infrequently, given the low rates of initial field resuscitation in their communities, so these systems of care are rarely experienced or optimized.

Some of the important elements of an effective post–cardiac arrest care strategy are delivery of therapeutic hypothermia to selected comatose patients, coronary angiography when there is a high degree of suspicion of an acute ischemic trigger, early hemodynamic stabilization of the patient with the ability to effectively treat rearrest, reliable prognostication, and appropriate cardiac electrophysiological assessment and treatment before discharge. Case-control studies have evaluated the effectiveness of combinations of some of these treatments in a variety of settings.[6,7,11,35–37] All have reported improved outcomes compared with historical controls (Table 1).

Collectively, these studies demonstrate the efficacy of multifaceted hospital-based interventions in patients resuscitated from OOHCA. It is difficult to conclude which of these components is essential, given the observational nature of these studies. Therefore, we briefly review evidence of the effectiveness of individual components of post–cardiac arrest care below.

Individual Components of Effective Post–Cardiac Arrest Care

Therapeutic Hypothermia

Control of temperature during the initial hospital period after resuscitation from OOHCA is an important factor in recovery. Randomized trials demonstrated that in-hospital induction of mild hypothermia (33°C to 34°C) for 12 to 24 hours in comatose survivors resuscitated from VF improved survival and neurological recovery.[38–40] Case series that included patients with non-VF cardiac rhythms have also demonstrated favorable outcomes.[41–43] The absence of fever during the first 48 hours after ischemic brain injury is also associated with better outcome.[44,45] Therapeutic hypothermia has also been studied for treatment of traumatic brain injury. Although the effectiveness of hypothermia after traumatic brain injury remains controversial, less variable outcomes were obtained from centers where therapeutic hypothermia was used often.[46] This supports observations that patients with severe head injuries who are treated by neurocritical care specialists using protocol-driven care plans have better outcomes.[47] Unfortunately, such specialized care as therapeutic hypothermia is not readily available or used in all centers.

Early PCI

Up to 71% of patients with cardiac arrest have coronary artery disease, and nearly half have an acute coronary occlusion.[48–50] There is a high incidence (97%) of coronary artery disease in patients resuscitated from OOHCA who undergo immediate angiography and a 50% incidence of acute coronary occlusion.[48] However, the absence of ST elevation on a surface 12-lead electrocardiogram after resuscitation of circulation from cardiac arrest is not strongly predictive of the absence of coronary occlusion on acute angiography.[48] A case series of patients with unsuccessful field resuscitation suggested that in such patients, VF is more likely to be due to coronary disease than is asystole or pulseless electric activity.[51] An autopsy study compared case subjects who died within 6 hours of symptom onset due to ischemic heart disease and who were not seen by a physician within 3 weeks with control subjects who died within 6 hours of symptom onset due to natural or unnatural noncardiac causes. The control subjects were matched to case subjects by age, gender, and socioeconomic status.[52] Sudden ischemic death was defined as sudden death with ≥75% stenosis of the lumen (≥50% of diameter) of a coronary artery with no other cause on autopsy, including toxicological studies. Intraluminal thrombosis was observed in 93% of case subjects versus 4% of control subjects. Collectively, these studies suggest that patients who are resuscitated from out-of-hospital VF have a high likelihood of having an acute coronary occlusion.

The feasibility and efficacy of primary PCI in patients who survive cardiac arrest with STEMI have been well established.[7,8,34,48,53–56] The combination of mild therapeutic hypothermia with primary PCI is feasible, may not delay time to start of primary PCI in well-organized hospitals, and is associated with a good 6-month survival rate and neurological outcome.[7,11,53] Trials of fibrinolytic therapy in patients who require ongoing resuscitation from OOHCA have not demonstrated improved outcomes in the intervention group compared with the control group.[57,58]

Patients resuscitated from OOHCA with STEMI should undergo immediate angiography and receive PCI as needed. Immediate coronary angiography is reasonable for patients resuscitated from VF and may be considered in patients resuscitated from other initial rhythms who do not have a clear noncardiac cause of cardiac arrest. Risk adjustment for these situations may not be adequate with current approaches to comparison of outcomes after PCI, and this may serve as a disincentive to perform angiography at some sites. Patients who undergo early PCI after restoration of circulation from cardiac arrest should be reported separately and not included in public reports of collective door-to-balloon times or mortality rates. Because emergent coronary angiography is not widely available, patients resuscitated from out-of-hospital VF or from OOHCA with STEMI should be transported as soon as it is feasible to a facility that is capable of performing these procedures. Field providers treating such patients should bypass referral hospitals and go directly to a cardiac resuscitation receiving hospital so that these patients can receive angiography within 90 minutes. Air transport or stabilization in a referral hospital should be considered for patients with an anticipated time to angiography that exceeds 90 minutes.

Prognostication

Predicting long-term outcome after cardiac arrest is difficult.[59] Case series conducted before the era of therapeutic hypothermia identified clinical signs that predict poor outcome.[59–62] Recent reports of doubling of survival rates after hospital admission in some centers suggest that these signs have reduced reliability for assessment of prognosis in patients undergoing therapeutic hypothermia.[6,36] Neurological assessment of the prognosis in patients resuscitated from cardiac arrest and receiving induced hypothermia is unreliable during the initial post–cardiac arrest period (ie, 72 hours).[63] For example, patients resuscitated from cardiac arrest and treated with hypothermia who have motor responses no better than extension at day 3, formerly a predictor of poor outcome, can recover motor responses 6 days or more after the arrest and regain awareness.[64] Therefore, premature withdrawal of care from patients by providers who are unfamiliar with current approaches to assessment of post–cardiac arrest prognosis after use of hypothermia would limit the reduction in disability and death associated with cardiac arrest. These data also indicate the need for centers with systematic and modern intensive care for patients resuscitated from cardiac arrest to recalibrate the prognostic criteria for predicting outcome.[59]

Implantable Cardioverter-Defibrillators

ICDs decrease mortality in secondary prevention of OOHCA.[65–67] ICDs decrease mortality rates in survivors of cardiac arrest with good neurological recovery when treatable causes of arrest are not determined, in patients with underlying coronary disease without myocardial ischemia as the cause of arrest, and in patients with a low ejection

Table 2. Emerging Interventions for Cardiac Arrest

Intervention	Description	Rationale	Complexity
Early goal-directed therapy	Hemodynamic and oxygenation monitoring in combination with intravenous fluid and medication	Reduced reperfusion injury, organ dysfunction, and death. Decreased mortality compared with standard care in patients with sepsis,[74] which has physiological characteristics similar to those in patients resuscitated from cardiac arrest[75]	Need for invasive monitoring catheters, with consequent risk of hemorrhage and pneumothorax, or serial blood draws with consequent risk of hemorrhage and distal ischemia
Glucose control	Insulin therapy and frequent blood glucose monitoring to maintain glycemic control	Elevated serum glucose associated with poor outcome after cardiac arrest[76–78]	Strict glycemic control associated with increased incidence of accidental hypoglycemia[79]
Seizure control	Continuous EEG monitoring and antiepileptic drugs	Clinical seizures occur in 7% to 8% of patients resuscitated from cardiac arrest[38]; incidence of electrographic seizures unknown. Continuous EEG detects electrographic seizures associated with metabolic compromise to brain after trauma[80,81]	Thiopental and diazepam did not significantly improve clinical outcomes in patients resuscitated from cardiac arrest.[82,83] Current antiepileptic drugs not evaluated in patients resuscitated from cardiac arrest
Cardiopulmonary support	Hemodynamic support with or without oxygenation using a venous line, centrifugal pump head, with or without oxygenator/heat exchanger structure, and arterial line in combination with percutaneous cannulas	Myocardial dysfunction commonly observed after resuscitation.[84,85] Cardiopulmonary bypass during ongoing arrest associated with improved outcomes compared with historical controls[86]	New circulatory devices could be used to facilitate rapid cardiopulmonary support.[87–89] Need for specialized staff and equipment
Hemofiltration	Removes extracellular fluid by process similar to hemodialysis	In animal models of ischemia-reperfusion injury, hemofiltration improves myocardial performance, hemodynamics, and survival rates.[90–92] Results of small trial suggest hemofiltration could improve survival in humans resuscitated from cardiac arrest[93]	Need for specialized staff and equipment

EEG indicates electroencephalogram.

fraction (ie, <30% to 35%) in combination with medical therapy.[68,69] Despite such strong evidence of effectiveness, there are regional variations in rates of ICD implantation[70,71] according to the teaching status of the hospital and the patient's race.[72,73] A systematic approach to assessment of eligibility for ICD implantation is necessary to reduce these disparities. Thus, patients resuscitated from cardiac arrest should be assessed for their need for an ICD before discharge from hospital.

Emerging Interventions for Patients Resuscitated From Cardiac Arrest

Evidence is emerging of the potential effectiveness of several other interventions in patients resuscitated from cardiac arrest. Each of these interventions is a complex or technical procedure that likely requires special experience and expertise to ensure its success (Table 2). Cardiac resuscitation centers could develop expertise in the efficacious application of these interventions, contribute to accumulating knowledge of their effectiveness, and train others in their use.

Other Evidence Relevant to Cardiac Resuscitation Systems of Care

Relationship Between Case Volume and Outcome

The concept of regional systems of care for cardiac resuscitation is supported by multiple examples throughout the field of medicine of the positive correlation between greater provider experience or procedural volume for complex diagnoses or procedures and better patient outcome.[94] The relationship between volume and outcome is complex. Procedural volume is an identifiable surrogate marker for a number of patient, physician, and systems variables that have an impact on outcome but are difficult to quantify individually. The benefit of volume on outcome is noted in health conditions that involve a systems-based approach. These include the care of patients with conditions that require time-sensitive intervention, including in-hospital and out-of-hospital cardiac arrest,[3,95] OOHCA,[96] traumatic injury,[97] and patients with STEMI who undergo primary angioplasty.[98]

Trauma Systems of Care

Regionalization of care for patients with traumatic injuries has been evaluated in multiple observational studies (Appendix). Estimation of an overall effect of regionalization of trauma care is difficult because of the heterogeneity of study inclusion criteria, interventions, baseline characteristics of patients, and date of study performance. Also, the majority of these studies included only patients admitted to the hospital and so may be subject to some selection bias. Nonetheless, the majority of these studies suggest that implementation of regionalized trauma systems is associated with significant and important improvements in outcome for these conditions.

STEMI Systems of Care

Regionalization of care for those with acute myocardial infarction[19–21] has led to significant and important improvements in outcome. Pooled analyses of randomized trials have demonstrated that primary PCI can reduce rates of death, recurrent myocardial infarction, and hemorrhagic stroke compared with fibrinolysis for patients with acute STEMI.[99] For this reason, use of PCI in patients with STEMI is an American College of Cardiology/American Heart Association class I recommendation.[100] However, a majority of US hospitals lack PCI facilities that are active 24 hours a day, 7 days a week. For patients who are initially treated at these non-PCI centers, the results of recent observational and randomized trials support the efficacy of rapid triage and transport as being superior to on-site fibrinolytic therapy (Table 3). Because some provider skills and patient procedures are common between trauma, STEMI, and cardiac arrest patient populations, and the effectiveness of regionalization of trauma and STEMI care is well documented, regional cardiac resuscitation centers should usually be aligned with these systems of care.

Stroke Systems of Care

An organized regional stroke system of care in which fibrinolytic treatment is begun at the referral hospital and continued at the stroke center can provide high rates of treatment with fibrinolytic agents with low rates of symptomatic intracerebral hemorrhage and excellent functional outcome at 3 months.[109] Patients with acute stroke whose care is managed by a multidisciplinary team in a ward dedicated exclusively to acute, rehabilitative, and comprehensive stroke care are significantly less likely to die, be institutionalized, or be dependent than those who receive care from a mobile stroke team or within a generic disability service.[110]

The American Stroke Association, a division of the American Heart Association, has actively encouraged the development of regional systems of care for patients with stroke.[111] The Joint Commission worked with the American Stroke Association to establish a system for certification of primary stroke centers. As of April 2009, more than 500 hospitals across the United States are certified as stroke centers. The American Stroke Association also recommended the integration of EMS into stroke systems of care and recommended that EMS protocols encourage transport of stroke patients to primary stroke centers when feasible.[112]

Financial Issues

Societal resources are limited, and health care must be allocated efficiently.[113] Some may argue that the costs or charges associated with this multifaceted approach are likely to be excessive, but resuscitation interventions that are associated with increased rates of survival are also associated with improved quality of life[114–116] and acceptable cost to society.[117]

Regional EMS systems[118] and trauma systems of care[119] have been established throughout the United States with little dedicated funding. In most if not all regions, demand for emergency or trauma care exceeds the ability of hospitals to provide it. If reimbursements fail to cover emergency department and trauma costs, these costs are subsidized by revenue from admissions that originated in the emergency department. Such uncompensated care is a burden for hospitals with large numbers of uninsured patients.[120] Trauma centers experience collective losses of more than $1 billion annually due to a disproportionate and increasing share of patients without the means to pay, lack of ability to shift cost to finance trauma care, difficult relationships with managed care, no payment by Medicare for standby costs, and insufficient reimbursement by automobile insurers or state Medicaid programs. In some states, hospitals receive Disproportionate Share Hospital payments from both Medicare and Medicaid to compensate for these losses, but such payments are often inadequate for hospitals with large "safety net" populations. Some hospitals that provided emergency and trauma care have closed in recent years because of financial losses.[121]

Public and tertiary hospitals bear a large share of this burden, because surrounding community hospitals often transfer their most complex, high-risk patients to these safety net hospitals for specialized care. To ensure the continued viability of a critical public safety function, the Institute of Medicine has recommended that Congress establish dedicated funding to reimburse hospitals that provide significant amounts of uncompensated emergency and trauma care for their associated financial losses.

Medicare is likely to continue to experience difficulty in paying for standby costs; however, Medicare and other payers are introducing "payment for performance" for multiple chronic health conditions. Participation of EMS and cardiac resuscitation centers in the monitoring and reporting of the cardiac resuscitation process and outcome is a promising method of providing sufficient incentives for providers to improve cardiac resuscitation outcomes.

Successful implementation and maintenance of cardiac resuscitation systems of care will require increased funding for care provided by EMS, level 2/referring cardiac resuscitation centers, and level 1/receiving cardiac resuscitation centers. Such funding might be made possible through a system of shared reimbursement for systems of care, including payments to smaller referral hospitals that prepare and transfer these complex cases to the receiving hospital, to EMS for providing emergent interfacility transport with vigilance for rearrest, and to receiving hospitals that ultimately provide the bulk of post–cardiac arrest care. Such shared reimbursement should include provisions for pay for performance. If the system of care delivers better quality of care, then each component of the system should be rewarded.

We are aware that the transfer of a large number of patients from 1 hospital to another could have an adverse impact on the revenue of the referring hospital. Revenue shifting within a regional system could be reduced by transferring patients who have spontaneous circulation but

Table 3. Effect of Regional Systems of Care on Patients With STEMI

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator
Vermeer et al[101]: Individual randomized trial in 1 province, Netherlands	AMI, presenting at hospitals not capable of PPCI	Transfer for PPCI (n=75)	Fibrinolytic in non-PCI hospital (n=75)	Fibrinolytic with transfer; rescue PCI if indicated (n=74)
		Symptoms to therapy 240 min±NR	Symptoms to therapy 135 min±NR	Symptoms to therapy 255 min±NR
		Door to balloon NR	Door to balloon NR	Door to balloon NR
		Death* 5 (7)	Death* 5 (7)	Death* 6 (8)
		Recurrent infarct* 1 (1)	Recurrent infarct* 7 (9)	Recurrent infarct* 4 (5)
		Stroke* 2 (3)	Stroke* 2 (3)	Stroke* 3 (4)
Widimský et al[102]: Individual randomized trial in 1 province, Czech Republic	AMI, presenting within 6 h of symptom onset at hospitals not capable of PPCI	Immediate transfer for PPCI (n=101)	Fibrinolytic therapy in non-PCI hospitals (n=99)	Fibrinolytic therapy during transport for PCI (n=100)
		Symptoms to therapy 215 min±NR	Symptoms to therapy 132 min±NR	Symptom to therapy 220 min±NR
		Door to balloon NR	Door to balloon NR	Door to balloon NR
		Death† (7)	Death† (14)	Death† (12)
		Recurrent infarct† (1); *P*<0.03	Recurrent infarct† (10)	Recurrent infarct† (7)
		Stroke† (0)	Stroke† (1)	Stroke† (3)
Andersen et al[103]: Individual randomized trial in Denmark	AMI with ST elevation presenting at hospital not capable of PPCI	Transfer for angioplasty within 3 h (n=567)	Fibrinolysis at referral hospital (n=562)	N/A
		Symptoms to therapy 227 min±NR	Symptoms to therapy 150 min±NR	
		Door to balloon 26 min	Door to therapy NR	
		Death† 37 (7)	Death† 48 (9)	
		Recurrent infarct† 11 (2)	Recurrent infarct† 35 (6)	
		Stroke† 16 (2)	Stroke† 11 (2)	
Grines et al[104]: Individual randomized trial in the United States and Europe	High-risk AMI with ST elevation or presumed new left bundle-branch block <12 h	Transfer for PPCI (n=71)	Fibrinolytic therapy (n=66)	N/A
		Symptoms to therapy NR	Symptoms to therapy NR	
		Door to balloon 174 min±80	Door to therapy 63±39 min	
		Death† 6 (8)	Death† 8 (12)	
		Recurrent infarct† 1 (1)	Recurrent infarct† 0 (0)	
		Stroke† 0 (0)	Stroke† 3 (4)	
Bonnefoy et al[105]: Individual randomized trial in France	Patients with STEMI presenting to EMS within 6 h of symptom onset	PPCI (n=421)	Prehospital fibrinolysis (n=419)	N/A
		Symptoms to therapy NR	Symptoms to therapy NR	
		Death† 20 (5)	Death† 16 (4)	
		Recurrent infarct† 7 (2)	Recurrent infarct† 15 (4)	
		Stroke† 0 (0)	Stroke† 4 (1)	
Widimský et al[106]: Individual randomized trial in Czech Republic	Patients with STEMI within 12 h of symptom onset presenting to non–PCI-capable hospital	Immediate transfer for primary PCI (n=429)	Fibrinolytic in community hospital (n=421)	N/A
		Symptoms to therapy 203 min±NR	Symptoms to therapy 185 min±NR	
		Death† 29 (7)	Death† 42 (10)	
		Recurrent infarct† 6 (1)	Recurrent infarct† 13 (3)	
		Stroke† 1 (0)	Stroke† 9 (2)	

(*Continued*)

Table 3. Continued

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator
Ting et al[21]: Prospective cohort in 3 US states up to 150 miles from PCI-capable hospital	Patients with STEMI within 12 h of symptom onset	Presented at non-PCI capable hospital and transferred for PPCI (n=258)	Presented at PCI-capable hospital and underwent PPCI (n=105)	Presented at non-PCI hospital <3 h from symptom onset and given fibrinolytic drug (n=131)
		Symptoms to therapy 278 min (171, 601)	Symptoms to therapy 188 min (124, 389)	Symptoms to therapy 103 min (61, 145)
		Door to balloon 116 min (102, 137)	Door to balloon 71 min (56, 90)	In-hospital death 4 (3.1)
		In-hospital death 6 (5.7)	In-hospital death 17 (6.6)	Recurrent infarct 8 (6.1)
		Recurrent infarct 3 (2.9)	Recurrent infarct 4 (1.6)	Stroke 2 (0.8)
		Stroke 1 (1.0)	Stroke 2 (0.8)	
Henry et al[20]: Prospective cohort in 3 US states	Patients with STEMI or new left bundle-branch block within 24 h of symptom onset	Transfer for PCI at PCI-capable hospital (n=621)	Transfer for facilitated PCI at PCI-capable hospital‡ (n=421)	Primary PCI at PCI-capable hospital (n=297)
		Symptoms to therapy 203 min (147, 325)	Symptoms to therapy 214 min (167, 326)	Symptoms to therapy 171 min (118, 307)
		Door to balloon 95 min (82, 116)	Door to balloon 120 min (100, 145)	Door to balloon 65 min (47, 84)
		In-hospital death 24 (3.8)	In-hospital death 22 (5.2), P=0.48	In-hospital death 11 (3.7)
		Recurrent infarct 5 (0.8)	Recurrent infarct 1 (0.2), P=0.02	Recurrent infarct 7 (2.4)
		Stroke 6 (1.0)	Stroke 5 (1.2), P=0.84	Stroke 4 (1.3)
Jollis et al[107]: Before-after year-long implementation in 1 state	Patients with STEMI	After implementation of statewide system for reperfusion (n=404 non-PCI; n=585 PCI)	Before implementation Control (n=518 non-PCI; n=579 PCI)	N/A
		Presentation to PCI hospital 74 min	Presentation to PCI hospital 85 min (P<0.001)	
		Transferred to PCI hospital 128 min	Transferred to PCI hospital 165 min (P<0.001)	
		Door-to-needle in non-PCI 29 min	Door-to-needle in non-PCI 35 min (P=0.002)	
		Door-in door-out non-PCI 71 min	Door-in-door-out non-PCI 120 min (P<0.001)	
		Nonreperfusion in non-PCI hospital 15%	Nonreperfusion in non-PCI hospital 15% (P not significant)	
		Nonreperfusion in PCI hospital 11%	Nonreperfusion in PCI hospital 23% (P not stated)	
		Death in PCI hospital 6.2%	Death in PCI hospital 7.5% (P=0.38)	
Le May et al[108]: Prospective cohort study in 1 city	Patients with STEMI	Referral from field by paramedics for PPCI (n=135)	Referral from ED by physicians for PPCI after interhospital transfer (n=209)	N/A

(*Continued*)

Table 3. Continued

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator
		Symptoms to balloon 158 min (116, 207)	Symptoms to balloon 230 min (173, 351)	
		Death 4 (3.0)	In-hospital death 12 (5.7)	
		Recurrent infarct 2 (1.5)	Recurrent infarct 2 (1.0)	
		Stroke 1 (0.7)	Stroke 3 (1.4)	

Values are expressed as n, n (%), or median (interquartile range), as appropriate.

AMI indicates acute myocardial infarction; ±NR, standard deviation not reported; NR, not reported; N/A, not applicable; and ED, emergency department.

*Outcomes at 42 days, not hospital discharge.

†Outcomes at 30 days, not hospital discharge.

‡Half-dose of tenecteplase given to fibrinolytic-eligible patient before transfer.

lack consciousness after cardiac arrest but not transferring patients who have spontaneous circulation and obey verbal commands. The latter group, who usually were resuscitated after VF followed by a short interval to defibrillation, do not need cooling. Instead, they warrant high-quality post–cardiac arrest care at a facility that is able to provide high-quality care for acute STEMI and subsequent assessment for ICD insertion. Such care may be available in the hospital that receives the patient first from the field.

We are also aware that the use of therapeutic hypothermia after cardiac arrest is currently not reimbursed by the Center for Medicare Services. We expect that as evidence of the effectiveness of hypothermia continues to accumulate, reimbursement for hypothermia will be reconsidered.

Knowledge Gaps

These interventions only address care in the hours and first days after resuscitation from cardiac arrest. Other important interventions to treat subsequent neurological injury, including physical rehabilitation and neuropsychiatric evaluation and treatment, remain to be studied carefully among postarrest patients but may provide significant benefit. Furthermore, the timing of additional cardiac interventions, such as placement of internal defibrillators, requires further investigation. Finally, an important source of variability in postarrest care is the limited validity of early prognostication of futility, especially when interventions such as hospital-based hypothermia are used. Valid approaches must be used to avoid premature prognostication of futility without causing an unnecessary burden on families and healthcare resources. Although evidence-based guidelines for prognostication after cardiac arrest have been published, these have not been validated in patients treated with therapeutic hypothermia.[59] Research is urgently needed to validate a reliable approach to prognostication in such patients.

Several unanswered questions remain, including (1) identification of the critical elements of a regional system required to achieve timely restoration of coronary artery blood flow; (2) determination of the impact of a regional cardiac resuscitation system of care on patients' health-related quality of life and costs; and (3) determination of the impact of regionalization on the economics of hospitals within these systems. There is insufficient evidence for or against regional systems of care for pediatric cardiac arrest. In addition, management of in-hospital cardiac arrest is an important issue, but we believe ongoing research is necessary to demonstrate the effectiveness of hypothermia, immediate angiography, and other interventions in such patients in order to consider how to respond to cardiac arrest in this setting.

Essential Elements of Regional Systems of Care for OOHCA

Treatment of the patient who has restoration of circulation after cardiac arrest is complex, occurs in both the out-of-hospital and in-hospital settings, is time sensitive, and depends on the coordinated actions of diverse healthcare providers, including EMS personnel, emergency medicine physicians, cardiologists, critical care physicians, nurses, and other key personnel.[34] A community-wide plan to optimize treatment sequentially from successful out-of-hospital resuscitation to hospital discharge should be implemented. A priori agreements between EMS and hospitals should be established with protocol-driven decisions to match patient needs with the capability of the transport-destination hospital to meet those needs. The content and timeliness of communication from EMS to hospitals should be addressed to proactively mobilize healthcare personnel before arrival and reduce time delays to treatment.

These efforts should not be the exclusive domain of academic medical centers. Regional systems may involve a town, a city, a county, a state, or another region of the country. Systems should include academic or community receiving hospitals with multidisciplinary teams, including cardiology, critical care, and neurology. The volume of patients who have restoration of circulation after cardiac arrest is not solely tied to specific institutions but to practitioners who practice at multiple institutions. Furthermore, referral hospitals will continue to play a vital role in optimizing care for patients with restoration of circulation after OOHCA. Their immediate efforts, before transfer to the receiving hospital, in initiating therapeutic hypothermia early in conjunction with EMS will be important in the final outcomes of many patients. Referral hospitals should be provided with the necessary funds for equipment and education and required to follow specific patient care and

Table 4. Essential Elements of Regional Systems of Care for OOHCA

EMS	Level 2 CRC	Level 1 CRC
Medical direction works with hospital to develop plan	Works with EMS medical direction to develop plan	Works with EMS medical direction to develop plan
		Aligned with STEMI centers
External certification not self-designation	External certification not self-designation	External certification not self-designation
	Initiates hypothermia as soon as feasible when indicated	Initiates hypothermia as soon as feasible when indicated
	Not capable of PPCI	Capable of PPCI
Field triage of patients with spontaneous circulation after OOHCA to level 1 CRC when feasible (eg, to allow angiography of catheterization-eligible patients within 90 min)	Early transport of patients resuscitated from OOHCA and transported from level 2 CRC to level 1 CRC (eg, via ground or air to allow angiography of catheterization-eligible patients within 90 min)	Hospital or most responsible physician group treats at least 40 patients resuscitated from OOHCA annually[96]; meets ACC/AHA STEMI guidelines for PPCI; resuscitation-related services available 24 hours a day, 7 days a week
Plan for and treat rearrest, including mechanical device or pharmacological support if appropriate	Plan for and treat rearrest, including mechanical device or pharmacological support if appropriate	Plan for and treat rearrest, including mechanical device or pharmacological support if appropriate
	Not capable of electrophysiology testing and ICD assessment and placement	Capable of electrophysiology testing and ICD assessment and placement
	Provides CPR training for lay public	Provides CPR training for lay public
	Provides CPR and ACLS training for staff	Provides CPR, ACLS, and PALS training for staff
		Defers assessment of prognosis to 72 h after arrest
Monitors, reports, and improves outcomes	Monitors, reports, and improves outcomes	Establishes and maintains multidisciplinary team including EMS, emergency medicine, nursing, cardiology, neurology, and critical care personnel, to monitor and improve resuscitation process and outcome
Reimbursed for participation	Reimbursed for participation	Reimbursed for participation

CRC indicates cardiac resuscitation centers; ACC/AHA, American College of Cardiology/American Heart Association; CPR, cardiopulmonary resuscitation; ACLS, advanced cardiovascular life support; and PALS, pediatric advanced life support.

triage protocols, and they should report their experience, as has been done in selected inclusive regional trauma systems.[122]

As with trauma centers, burn centers, STEMI centers, and stroke centers, national criteria should be developed to enable the categorization, verification, and designation of centers for the treatment of patients with restoration of circulation after OOHCA. External credentialing should be required as opposed to self-designation to support the development and sustainability of adequate patient volumes and high-quality care. The number of level 1 cardiac resuscitation centers in a given region should be limited to maintain provider skill levels and to justify the initial costs and institutional commitment required to care for these specialized patients. Assessments of provider or hospital performance of acute coronary angiography should separate procedures performed in patients resuscitated from cardiac arrest from those performed in other patients to reduce potential disincentives to the performance of an intervention in these patients with high morbidity and mortality. Evidence-based best practices and model EMS protocols should also be developed to guide states and local EMS systems in developing inclusive regionalized approaches to postresuscitation care.

We propose interim criteria for regional systems of care for patients resuscitated from OOHCA (Table 4). On the basis of our consensus review of the published scientific literature related to OOHCA and other acute life-threatening illnesses, we believe that the time has come for a call to develop and implement standards for regional systems of care for those with restoration of circulation after OOHCA; concentrate specialized postresuscitation skills in selected hospitals; transfer unconscious post–cardiac arrest patients to these hospitals as appropriate; monitor, report, and try to improve cardiac resuscitation structure, process, and outcome; and reimburse these activities. Furthermore, we propose 2 levels of cardiac resuscitation centers, with transfer of patients with spontaneous circulation after OOHCA who remain unconscious from level 2 to level 1 centers. These interim criteria should be reevaluated periodically as new evidence of the effectiveness of resuscitation care accumulates. Successful implementation and maintenance of cardiac resuscitation systems of care would have a significant and important impact on the third-leading cause of death in the United States. The time to implement these systems of care is now.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Graham Nichol	University of Washington-Harborview Medical Center	Resuscitation Outcomes Consortium (NIH U01 HL077863–05) 2004–2009, Co-PI†; Randomized Trial of CPR Training Aid (Asmund S. Laerdal Foundation for Acute Medicine), PI*; Randomized Trial of Hemofiltration After Resuscitation from Cardiac Arrest (NHLBI R21 HL093641–01A1) 2009–2011, PI†; Randomized Field Trial of Cold Saline IV After Resuscitation from Cardiac Arrest (NHLBI R01 HL089554–03) 2007–2012, Co-PI†	None	None	None	None	None	American Heart Association*; Collaborator, Resynchronization in Advanced Failure (RAFT) Trial [CIHR, Medtronic Inc]*; Co-PI, Resuscitation Outcomes Consortium Data Coordinating Center [NHLBI, CIHR, US Department of Defense, Heart and Stroke Foundation of Canada]*; Laerdal Inc*; Physio-Control Inc*; Channing Bete Inc*
Benjamin S. Abella	University of Pennsylvania, Assistant Professor	National Insitutes of Health; Philips Medical Systems†; Cardiac Science Corporation†	Laerdal Medical Corporation*	Philips Medical Systems*; Alsius Corporation*; Medivance Corporation*; Gaymar Corporation*	None	None	Philips Medical Systems*	None
Tom P. Aufderheide	Medical College of Wisconsin Medical University, Professor of Emergency Medicine	Resuscitation Outcomes Consortium, Principal Investigator of the Milwaukee study site†; Neurological Emergency Treatment Trials (NETT) Network, Principal Investigator of the Milwaukee study site†; ResQTrial (NHLBI/Advanced Circulatory Systems), Principal Investigator of the Oshkosh study site*; Immediate Trial (NHLBI), Principal Investigator of the Milwaukee study site*	Zoll Medical*; Advanced Circulatory Systems Inc*	EMS Today*	None	None	Take Heart America†; Medtronic, Inc*; JoLife*	None
Robert R. Bass	State of Maryland; Maryland Institute for EMS Systems	None	None	None	None	None	None	None
Vincent J. Bufalino	Midwest Heart Specialists	None	None	None	Expert witness on several cases per year over the past 6–8 years*	None	United Healthcare Scientific Advisory Board*	None

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Writing Group Disclosures, Continued

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Clifton W. Callaway	University of Pittsburgh and UPMC Health System School of Medicine Healthcare Network	Resuscitation Outcomes Consortium (U01 HL077871) 2004–2009†; Hypothermia and Gene Expression after Cardiac Arrest (R01 N5046073) 2002–2006†; American Heart Association Grant-in-Aid (0755359U) on cerebrovascular effects on thrombin activation after cardiac arrest†	Medivance, Inc*	None	None	Coinventor on patents related to ventricular fibrillation waveform analysis (1 patent licensed by University of Pittsburgh to Medtronic ERS, Inc, a manufacturer of defibrillators)†	None	None
Cynthia M. Dougherty	University of Washington	None	None	None	None	None	None	None
Brian Eigel	American Heart Association	None	None	None	None	None	None	None
Monica E. Kleinman	Children's Hospital Anesthesia Foundation	None	None	None	None	None	None	None
Keith G. Lurie	St. Cloud Hospital, Hennepine County Medical Center, Advanced Circulatory Systems Inc	None	None	None	None	Inventor of the ResQPOD†	None	None
Venugopal Menon	Cleveland Clinic Hospital	None	None	None	None	None	None	None
Robert W. Neumar	University of Pennsylvania	NIH-NINDS, R21NS054654, Title: Optimizing Therapeutic Hypothermia After Cardiac Arrest, PI: Neumar, June 2005–May 2010†; NIH-NINDS, R01NS039481, Title: Calpain-Mediated Injury in Post-Ischemic Neurons, PI: Neumar, June 2005–April 2010†	None	None	None	None	None	None
Robert E. O'Connor	University of Virginia Health System	None	None	None	None	None	None	None
Eric W. Ossmann	Emory University	None	None	None	Expert witness in a cardiac arrest–related case*	None	None	None
Eric Peterson	Duke University	None	None	None	None	None	None	None
Edward M. Racht	Piedmont Newnan Hospital	None	None	None	None	None	Vidacare Scientific Advisory Board*	None
John P. Reilly	Ochsner Health System Hospital	None	None	Cordis (Johnson & Johnson)*; Eli Lilly/Daiichi Sankyo*	None	None	None	None
Michael Sayre	Ohio State University, Associate Professor of Emergency Medicine	Laerdal Foundation for Acute Medicine†	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Ben Bobrow	Arizona Department of Human Services	None	None	None	None	None	None	None
Karl Kern	University of Arizona	Laerdal Foundation Grant†	None	None	Case involving postresuscitation myocardial dysfunction†	None	ZOLL Medical†; Medtronic PhysioControl*	None
Mary Elizabeth Mancini	The University of Texas at Arlington	None	None	None	None	None	None	None
Joe Ornato	Virginia Commonwealth University Health System	None	None	None	None	None	AHA's NRCPR*	None
Tom Rea	University of Washington	None	None	None	None	None	None	None

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*Modest.

†Significant.

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Appendix. Effect of Regional Systems of Care on Patients With Traumatic Injury

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Abernathy et al[123]: Retrospective cohort study of administrative data	Patients from 6 counties in Alabama transported by EMS and admitted to level 1 trauma center from April 1995 to March 1998	Implementation of voluntary regional trauma system n=1718 Mortality: 65 (3.8%) ISS ≥16: 342 (20%) Adjusted OR or RR not reported	Before implementation n=1306 Mortality: 77 (5.9%), P=0.0002 ISS ≥16: 276 (21%)	N/A	N/A
Boyd et al[124]: Retrospective cohort study of hospital-based trauma registries	Patients with motor vehicle–related injuries from 14 counties in Region 13A, Illinois, from July 1970 to December 1972	Implementation of regional trauma program n=15 061 ISS not reported Mortality: 2.5% Adjusted OR or RR not reported	Before implementation n=13 459 ISS not reported Mortality: 2.7%	N/A	N/A

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Appendix, Continued

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Culica et al[125]: Retrospective cohort study of administrative data	Injured patients hospitalized in trauma centers in Texas from 1999 to 2000	Admitted to level 1 (n=35 878) Mortality: 1514 (57.4%) Adjusted OR* 0.31 (95% CI 0.27–0.36)	Admitted to level 2 (n=15 300) Mortality: 603 (22.9%) Adjusted OR* 0.47 (95% CI 0.4–0.55)	Admitted to level 3/4 (n=31 669) Mortality: 520 (19.7%) Reference group, $P<0.0001$	N/A
de Jongh et al[126]: Retrospective cohort study of regional trauma registry	Trauma admissions, dead on arrival, or died in ED at 12 EDs in Netherlands from 2000 to 2006	Transferred from another hospital to trauma center (n=69) ISS, median (IQR) 25 (17–26) Mortality: 21.7% Referent group	Direct admissions to nontrauma center (n=448) ISS, median (IQR) 19 (16–25) Mortality: 13.6% Adjusted OR† 1.5 (95% CI 0.7–3.4)	Direct admissions to trauma center (n=382) ISS, median (IQR) 25 (17–30) Mortality: 28.8% Adjusted OR† 1.9 (95% CI 0.9–4.1)	N/A
Hannan et al[127]: Retrospective cohort study of state trauma registry	Injured, age >13 y identified in prehospital care reports, >1 trauma triage criterion, transported directly to hospital. Excluded patients with flat vital signs on arrival at ED. From 1996 to 1998	Level 1 trauma center (n=2218) ISS not reported Mortality: 46.8% Referent group Unadjusted OR 0.79 (95% CI 0.65–0.95)	Level 2 trauma center or nontrauma center (n=2525) ISS not reported Mortality: 53.2% Referent group	N/A	N/A
Harrington et al[128]: Retrospective cohort study of hospital trauma registry	Trauma patients admitted to single level 1 trauma hospital from 2001 to 2003	Direct transfer from field (n=3227) ISS 11±0.2 Mortality: 7% OR or RR not reported	Transfer from nontrauma center (n=280) ISS 17.5±0.8 Mortality: 10%	N/A	N/A
Liberman et al[129]: Retrospective cohort study of provincial trauma registry	Major trauma treated at hospital, including ≥1 death as result of injury, admission with hospital stay ≥3 days, admission to intensive care or interhospital transfer during 1992 to 1993 (before) and 2001 to 2002 (after)	After designation of level 1 trauma centers, triage, and transfer protocols (n=1884) ISS not reported Mortality: 8.6% OR or RR not reported	Before implementation of regional trauma care (n=3823) ISS not reported Mortality: 51.8%	N/A	N/A
MacKenzie et al[18]: Prospective stratified sample of cases and controls using medical record review and patient interview	Injured patients 18 to 84 y of age with ISS >15 treated at hospital in 15 contiguous Metropolitan Statistical Areas (n=5191). Excluded patients dead on arrival or within 30 min	Level 1 trauma centers Observed in-hospital mortality: 8% Adjusted mortality within 1 y: 10.4% Adjusted RR 0.75 (95% CI 0.6–0.95)	Nontrauma centers that treated >25 patients with trauma annually Observed in-hospital mortality: 5.9% Adjusted mortality within 1 y: 13.8%	N/A	N/A
Mann et al[130]: Retrospective cohort study of hospital discharge data linked with death index	Age >65 y discharged from acute care hospital who had ≥1 injury-related *ICD-9* discharge diagnosis in Washington from 1988 to 1995	After implementation of statewide trauma system (n=46 424) ISS 7.1±4.2 Mortality within 60 days: 10.4% Adjusted mortality 5.1% lower among patients with ISS >15‡	Before implementation (n=30 712) ISS 6.8±4.4 Mortality within 60 days: 10.1%	N/A	N/A
Mullins et al[131]: Retrospective cohort study of hospital discharge data linked with death index	Patients discharged from acute care hospital who had ≥1 injury-related *ICD-9* discharge diagnosis in Oregon (n=27 633) from 1985 to 1987 (before) and 1991 to 1993 (after)	After implementation of regional trauma system Adjusted OR for mortality§ 0.82 (95% CI 0.73–0.92)	Before implementation	N/A	N/A

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Appendix, Continued

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Mullins et al[132]: Retrospective cohort study of hospital discharge data linked with death index	Patients discharged from acute care hospital who had ≥1 injury-related *ICD-9* discharge diagnosis in Oregon and Washington from 1990 to 1993	Regional trauma system in Oregon (n=11 879) Adjusted OR for mortality‖ 0.80 (95% CI 0.70–0.91)	Regional trauma system in Washington (n=17 369)	N/A	N/A
Mullins et al[133]: Retrospective cohort study of hospital discharge data and hospital trauma registry	Patients discharged from acute care hospital who had ≥1 injury-related *ICD-9* discharge diagnosis in 4 counties in Oregon (n=27 633) from 1984 to 1985 (before), 1986 to 1987 (during), and 1990 to 1991 (after)	After implementation of regional trauma system Level 1 center (n=7238) Applicant trauma hospitals (n=4815) Nontrauma hospitals (n=9753) ISS not reported All hospitals adjusted OR for mortality¶ 0.94 (95% CI 0.82–1.07) compared with reference period	During implementation of regional trauma system Level 1 center (n=5017) Applicant trauma hospitals (n=6691) Nontrauma hospitals (n=11 691) ISS not reported All hospitals adjusted OR for mortality¶ 1.01 (95% CI 0.88–1.16) compared with reference period	Before implementation of regional trauma system Level 1 center (n=4239) Applicant trauma hospitals (n=6812) Nontrauma hospitals (n=14 094) ISS not reported Reference period	N/A
Mullner et al[134]: Retrospective cohort study of sample from Department of Transportation records of motor vehicle–related trauma	Patients with severe or fatal trauma in Region 5, Illinois, during and 1970 to 1973 (after)	Implementation of regional trauma system Regional trauma hospitals (n=958): ISS not reported Mortality: 8.5% Nontrauma hospitals (n=1676): ISS not reported Mortality: 11.4% OR or RR not reported	Before implementation Regional trauma hospitals (n=992): ISS not reported Mortality: 11.5% Nontrauma hospitals (n=1866): ISS not reported Mortality: 11.5%	N/A	N/A
Nathens et al[135]: Retrospective cohort study of National Center for Health Statistics data, FARS database, and census data	Deaths associated with unintentional injury or injury purposely inflicted by other persons. FARS motor vehicle–related deaths during 1995	States with functional trauma systems Deaths per 100 000 population All injuries: 26.5±16.0 Incident rate ratio 0.91 (95% CI 0.89–0.92) MVC-related injuries: 17.3±10.2 Incident rate ratio 0.82 (95% CI 0.81–0.84)	States without functional trauma systems Deaths per 100 000 population All injuries: 29.2±17.2 MVC-related injuries: 14.2±8.8	N/A	N/A
Nathens et al[136]: Retrospective cohort study of regional trauma registry	Trauma patients age ≥16 y injured in King County, Wash, from 1995 to 1998. Included if length of stay >2 days; *ICD* injury-related code; dead on arrival or died in hospital; interhospital transfer; or trauma team activation	Field triage to level 1 trauma hospital by medics (n=4439) ISS 11.7±12.9 Mortality: 10%	Field triage to level 3 or 4 trauma hospital by medics, then transfer to level 1 hospital after initial assessment (n=281) ISS 8.9±7.0 Mortality: 5% Adjusted RR for mortality# 1.05 (95% CI 0.61–1.80) compared with reference period	N/A	N/A

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Appendix, Continued

Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Nicholl et al[137]: Prospective before-after study using individual patient data	Trauma patients with ISS>15 brought directly to ED by ambulance or other means, whether or not vital signs present on arrival, from 1990 to 1993	Implementation of regional trauma system in northwest Midlands with 1 central hospital and on-site neurosurgery, 6 regional hospitals, 1 EMS agency Mortality: Before (n=502) 35%, after (n=409) 34% Adjusted difference in change in mortality between intervention and control per year** 0.8% (95% CI 3.6–2.2%)	No change in trauma care in Lancashire with 1 central hospital and on-site neurosurgery but no cardiothoracic surgery, 5 regional hospitals, 3 EMS agencies Mortality: Before (n=620) 35%, after (n=617) 33%	No change in trauma care in Humberside with 1 central hospital and on-site neurosurgery but no cardiothoracic surgery, 3 regional hospitals, 1 EMS agency Data combined with Lancashire	N/A
Potoka et al[138]: Retrospective cohort study of state trauma registry	Trauma patients ≤16 y old treated at accredited trauma center from 1993 to 1997. Excluded injuries due to burns	Transported to pediatric trauma center (n=5189) ISS >15: 11.9% Mortality: Blunt trauma 11.3%, penetrating trauma 21.3%	Transported to level 1 adult trauma center with additional qualifications (n=3636) ISS >15: 12.4% Mortality: Blunt trauma 11.4%, penetrating trauma 28.1%	Transported to level 1 adult trauma center (n=1207) ISS >15: 21.6% Mortality: Blunt trauma 13.0%, penetrating trauma 46.3%	Transported to level 2 adult trauma center (n=3319): ISS >15: 16.2% Mortality: Blunt trauma 14.1%, penetrating trauma 40.9%
Reilly et al[139]: Retrospective cohort study of hospital discharge data	Adult trauma patients discharged from New York City hospital from 1998 to 2000 (n=103 659). Excluded injuries due to burns	Hospitalized at level 1 trauma hospital (n=50 021) ISS not reported Mortality: 2.6% Adjusted odds of mortality in trauma hospital†† 1.8 (95% CI 1.7–2.0)	Hospitalized at other hospitals (n=53 704) ISS not reported Mortality: 1.9%	N/A	N/A
Sampalis et al[140]: Retrospective cohort study of hospital discharge data	Trauma patients transported by EMS and admitted to hospital during 1987 and 1993	Designation of receiving hospitals as level 1 trauma center (n=288) ISS 15.5±11.6 Mortality: 10% Adjusted odds of mortality before designation‡‡ 3.3 (95% CI 1.6–6.5)	Before designation (n=158) ISS 15.0±12.3 Mortality: 20%	N/A	N/A
Young et al[141]: Retrospective cohort study of hospital trauma registry	Adult trauma patients with ISS >15 admitted to trauma center	Direct transfer to level 1 trauma center (n=165) ISS 24±8 Mortality before discharge: 21% Adjusted odds of mortality not reported	Transfer from another hospital (n=151) ISS 23±7 Mortality before discharge: 18.5%	N/A	N/A
Clemmer et al[142]: Retrospective cohort study of regional trauma registry	Trauma patients transported by EMS with field CRAMS score ≤6. Excluded patients transported for >15 min and interfacility transports	Transported to level 1 trauma center (n=57) Mortality before discharge: 46% Adjusted odds of mortality not reported	Transported to local hospital (n=33) Mortality before discharge: 61%	N/A	N/A
Goldberg et al[143]: Retrospective cohort study of hospital discharge data	Trauma patients hospitalized in Illinois outside Chicago with selected injuries during 1973 and 1974	Hospitalized at trauma system hospitals (n=4560) Mortality before discharge: 2.9% Adjusted odds of mortality not reported	Hospitalized at nontrauma hospitals (n=5465) Mortality before discharge: 2.7%	N/A	N/A

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Authors/Reference: Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Hulka et al[144]: Retrospective cohort study of hospital discharge data	Children age ≤18 y with acute injury hospitalized in Oregon from 1985 to 1993	Before (n=14 082, 1985 to 1987) and after (n=8981, 1991 to 1993) implementation of statewide trauma system in Oregon Mortality: Before 0.96%, after 1.2% Adjusted odds of mortality not reported	Before (n=18 525, 1985 to 1987) and after (n=12 991, 1991 to 1993) No implementation of statewide trauma system in Washington Mortality: Before 0.93%, after 1.2%	N/A	N/A
Kane et al[145]: Retrospective cohort study of hospital discharge data	Injured <48 h before ED admission, ISS >15, admitted to or died at acute hospital in Los Angeles County from 1982 to 1984. Excluded injuries limited to drowning, smothering, strangulation, choking, hanging, electrical shock, asphyxiation, or spontaneous pathological fracture	After (n=766, 1984) implementation of countywide trauma system Mortality: 30.7% Adjusted odds of survival compared with before§§ 1.351 (95% CI 0.917–1.988)	Before (n=658, 1982) implementation of countywide trauma system Mortality: 29.5%	N/A	N/A
Mullner et al[146]: Retrospective cohort study of state trauma registry	Patients injured in MVC in southern Illinois from 1970 to 1973	After implementation of regional trauma system at trauma hospitals (n=958) and other hospitals (n=1676) Mortality at trauma hospitals: 8.5% Mortality at other hospitals: 11.4% Adjusted odds of mortality not reported	Before implementation of regional trauma system at trauma hospitals (n=992) and other hospitals (n=1866) Mortality at trauma hospitals: 11.5% Mortality at other hospitals: 11.5%	N/A	N/A
Norwood et al[147]: Retrospective cohort study of regional trauma registry	Injured patients who underwent surgery, died in ED, or were admitted to level 2 trauma hospital in east Texas from 1987 to 1992	After implementation of level 2 designation at trauma hospital (n=699) Mortality: 7.7% Adjusted odds of mortality not reported	Before implementation of level 2 designation at trauma hospital (n=862) Mortality: 8.0% Adjusted odds of mortality not reported	N/A	N/A
Sampalis et al[148]: Retrospective cohort study of hospital discharge data combined with census data	Patients with acute injury treated at tertiary trauma centers in Quebec from 1993 to 1995	Field transfer to tertiary trauma hospitals (n=2756) Mortality: 4.8%	Transfer from lower-level hospital to tertiary trauma hospital (n=1608) Mortality: 9.8% Adjusted odds of mortality‖‖ compared with field transfer 1.57 (95% CI 1.17–2.11	N/A	N/A

ISS indicates Injury Severity Score; OR, odds ratio; RR, relative risk; CI, confidence interval; IQR, interquartile range; FARS, Fatality Analysis Reporting System; MVC, motor vehicle collision; CRAMS, circulation, respiration, abdomen, motor, speech; and *ICD-9*, *International Classification of Diseases version 9*.

*Adjusted for age, race, insurance status, hospital stay >1 week, emergency admission, severity of injury, and risk of mortality.

†Adjusted for age, ISS, Glasgow Coma Scale score, and severe neurological trauma.

‡Adjusted for age, sex, injury severity, and comorbidity.

§Adjusted for age, sex, multiple injuries, Abbreviated Injury Score, and preexisting conditions.

‖Adjusted for age, sex, anatomic site, severity of injury, and preexisting conditions.

¶Adjusted for age, sex, Abbreviated Injury Score, and preexisting conditions.

#Adjusted for age, ISS, severity of head injury, maximum Abbreviated Injury Score, shock, and payer status.

**Adjusted for age, ISS, and Revised Trauma Score.

††Adjusted for age, sex, and severity of injury.

‡‡Adjusted for age, ISS, and mechanism of injury.

§§Adjusted for age, sex, hypotension, status of head injury, and mechanism of injury.

‖‖Adjusted for age, head and injury status, status of extremity injury, and Injury Severity Score.